

SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT: LIN, LEU-FEN
 COLLINS, FRANKLIN D.
 DOHERTY, DANIEL H.
 LILE, JACK
 BEKTESH, SUSAN

(ii) TITLE OF INVENTION: Glial Cell Line-Derived
 Neurotrophic Factor

(iii) NUMBER OF SEQUENCES: 26

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: AMGEN INC.
 (B) STREET: One Amgen Center Drive
 (C) CITY: Thousand Oaks
 (D) STATE: California
 (E) COUNTRY: USA
 (F) ZIP: 91320-1789

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy Disk
 (B) COMPUTER: IBM Compatible
 (C) OPERATING SYSTEM: 7.1
 (D) SOFTWARE: Microsoft Word for WIN 7.0a

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: 08/452,229
 (B) FILING DATE: 26-MAY-1995

(2) INFORMATION FOR SEQ ID NO:1

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(v) FRAGMENT TYPE: N-terminal fragment

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser Pro Asp Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Xaa
 5 10 15

Gln Ala Ala Ala Ala Ser Pro Asp Asn
 20 25

(2) INFORMATION FOR SEQ ID NO:2

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 13 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(v) FRAGMENT TYPE: internal fragment

(ix) FEATURE: Xaa is either Lys or Gln

099919 644660

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Asp Xaa Ile Leu Lys Asn Leu Gly Arg Val Arg Arg Leu
5 10

(2) INFORMATION FOR SEQ ID NO:3

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 900 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: nucleic acid for rat GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CCCCCGGGCT GCAGGAATTC GGGG GTC TAC GGA GAC CGG ATC CGA GGT 48
Val Tyr Gly Asp Arg Ile Arg Gly
-90

GCC GCC GCC GGA CGG GAC TCT AAG ATG AAG TTA TGG GAT GTC GTG 93
Ala Ala Ala Gly Arg Asp Ser Lys Met Lys Leu Trp Asp Val Val
-85 -80 -75

GCT GTC TGC CTG GTG TTG CTG CAC ACC GCG TCT GCC TTC CCG CTG 138
Ala Val Cys Leu Val Leu Leu His Thr Ala Ser Ala Phe Pro Leu
-70 -65 -60

CCC GCC GGT AAG AGG CTT CTC GAA GCG CCC GCC GAA GAC CAC TCC 183
Pro Ala Gly Lys Arg Leu Leu Glu Ala Pro Ala Glu Asp His Ser
-55 -50 -45

CTC GGC CAC CGC CGC GTG CCC TTC GCG CTG ACC AGT GAC TCC AAT 228
Leu Gly His Arg Arg Val Pro Phe Ala Leu Thr Ser Asp Ser Asn
-40 -35 -30

ATG CCC GAA GAT TAT CCT GAC CAG TTT GAT GAC GTC ATG GAT TTT 273
Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp Phe
-25 -20 -15

ATT CAA GCC ACC ATC AAA AGA CTG AAA AGG TCA CCA GAT AAA CAA 318
Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp Lys Gln
-10 -5 1 5

GCG GCG GCA CTT CCT CGA AGA GAG AGG AAC CGG CAA GCT GCA GCT 363
Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala
10 15 20

GCC AGC CCA GAG AAT TCC AGA GGG AAA GGT CGC AGA GGC CAG AGG 408
Ala Ser Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg
25 30 35

[illegible]

(2) INFORMATION FOR SEQ ID NO:4

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 134 amino acid residues
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: inferred amino acid sequence for mature rat GDNF
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Ser Pro Asp Lys Gln Ala Ala Ala Leu Pro Arg Arg Glu Arg Asn Arg
1 5 10 15
Gln Ala Ala Ala Ala Ser Pro Glu Asn Ser Arg Gly Lys Gly Arg Arg
20 25 30

Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu
 35 40 45
 Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile
 50 55 60
 Phe Arg Tyr Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr Met Tyr Asp
 65 70 75 80
 Lys Ile Leu Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr Ser Asp Lys
 85 90 95
 Val Gly Gln Ala Cys Cys Arg Pro Val Ala Phe Asp Asp Asp Leu Ser
 100 105 110
 Phe Leu Asp Asp Ser Leu Val Tyr His Ile Leu Arg Lys His Ser Ala
 115 120 125
 Lys Arg Cys Gly Cys Ile
 130

(2) INFORMATION FOR SEQ ID NO:5

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 562 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: nucleic acid sequence for human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATTT TCTCTTTTCT TTTTGAACAG CA AAT ATG CCA GAG GAT TAT CCT 47
 Ser Asn Met Pro Glu Asp Tyr Pro
 -25 -20

 GAT CAG TTC GAT GAT GTC ATG GAT TTT ATT CAA GCC ACC ATT 89
 Asp Gln Phe Asp Asp Val Met Asp Phe Ile Gln Ala Thr Ile
 -15 -10

 AAA AGA CTG AAA AGG TCA CCA GAT AAA CAA ATG GCA GTG CTT 131
 Lys Arg Leu Lys Arg Ser Pro Asp Lys Gln Met Ala Val Leu
 -5 1 5

 CCT AGA AGA GAG CGG AAT CGG CAG GCT GCA GCT GCC AAC CCA 173
 Pro Arg Arg Glu Arg Asn Arg Gln Ala Ala Ala Ala Asn Pro
 10 15 20

 GAG AAT TCC AGA GGA AAA GGT CGG AGA GGC CAG AGG GGC AAA 215
 Glu Asn Ser Arg Gly Lys Gly Arg Arg Gly Gln Arg Gly Lys
 25 30 35

009911611560

AAC CGG GGT TGT GTC TTA ACT GCA ATA CAT TTA AAT GTC ACT	257
Asn Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn Val Thr	
40 45 50	
GAC TTG GGT CTG GGC TAT GAA ACC AAG GAG GAA CTG ATT TTT	299
Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe	
55 60 65	
AGG TAC TGC AGC GGC TCT TGC GAT GCA GCT GAG ACA ACG TAC	341
Arg Tyr Cys Ser Gly Ser Cys Asp Ala Ala Glu Thr Thr Tyr	
70 75	
GAC AAA ATA TTG AAA AAC TTA TCC AGA AAT AGA AGG CTG GTG	383
Asp Lys Ile Leu Lys Asn Leu Ser Arg Asn Arg Arg Leu Val	
80 85 90	
ACT GAC AAA GTA GGG CAG GCA TGT TGC AGA CCC ATC GCC TTT	425
Ser Asp Lys Val Gly Gln Ala Cys Cys Arg Pro Ile Ala Phe	
95 100 105	
GAT GAT GAC CTG TCG TTT TTA GAT GAT AAC CTG GTT TAC CAT	467
Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu Val Tyr His	
110 115 120	
ATT CTA AGA AAG CAT TCC GCT AAA AGG TGT GGA TGT ATC TGA	509
Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys Ile	
125 130	
CTCCGGCTCC AGAGACTGCT GTGTATTGCA TTCCTGCTAC AGTGCAAAGA	559
AAG	562

(2) INFORMATION FOR SEQ ID NO:6

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 134 amino acid residues
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: inferred amino acid sequence for mature human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Ser	Pro	Asp	Lys	Gln	Met	Ala	Val	Leu	Pro	Arg	Arg	Glu	Arg	Asn	Arg
1				5					10					15	
Gln	Ala	Ala	Ala	Ala	Asn	Pro	Glu	Asn	Ser	Arg	Gly	Lys	Gly	Arg	Arg
			20					25					30		
Gly	Gln	Arg	Gly	Lys	Asn	Arg	Gly	Cys	Val	Leu	Thr	Ala	Ile	His	Leu
		35					40					45			

(2) INFORMATION FOR SEQ ID NO:7

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: oligonucleotide probe
 - (D) OTHER INFORMATION: N at positions 3, 15, and 18 is inosine
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

(2) INFORMATION FOR SEQ ID NO:8

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 223 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: nucleic acid sequence for human GDNF
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTG	GTG	CTG	CTC	CAC	ACC	GCG	TCC	GCC	TTC	CCG	CTG	CCC	GCC	130
Leu	Val	Leu	Leu	His	Thr	Ala	Ser	Ala	Phe	Pro	Leu	Pro	Ala	
				15					20					

GGC CGC CGC CGC GCG CCC TTC GCG CTG AGC AGT GAC T 209
Gly Arg Arg Arg Ala Pro Phe Ala Leu Ser Ser Asp
40 45 50

(2) INFORMATION FOR SEQ ID NO:9

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 12 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ix) FEATURE:
 - (A) NAME/KEY: linker

CCCGAATTCG GG 12

Pro Asp Lys Gln Ala Ala Ala
5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

(2) INFORMATION FOR SEQ ID NO:12
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acid residues
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Glu Arg Asn Arg Gln Ala Ala Ala Ala Ser Pro
5 10

(2) INFORMATION FOR SEQ ID NO:13

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide DHD-26
- (D) OTHER INFORMATION: N at positions 9 and 12 are inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ARRTTYTTNA RNATYTTRTC

20

(2) INFORMATION FOR SEQ ID NO:14

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acid residues
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Asp Lys Ile Leu Lys Asn Leu
5

(2) INFORMATION FOR SEQ ID NO:15

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

GACGGGACTC TAAGATG

17

(2) INFORMATION FOR SEQ ID NO:16

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE

- (A) NAME/KEY: oligonucleotide primer DHD23

(D) OTHER INFORMATION: N at positions 3, 6, and 18 is inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

GCNGCNGCYT GYTTRTCNGG

20

(2) INFORMATION FOR SEQ ID NO:17

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer LF2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

CGAGACAATG TACGACA

17

(2) INFORMATION FOR SEQ ID NO:18

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CTCTGGAGCC AGGGTCA

17

(2) INFORMATION FOR SEQ ID NO:19

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: oligonucleotide primer PD1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

CCCGAATTCG ACGGGACTCT AAGATG

26

(2) INFORMATION FOR SEQ ID NO:20

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ix) FEATURE:

T.O.T.T. 6 F F 6 6 6 0

(A) NAME/KEY: oligonucleotide primer LFA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

CGGTGGCCAG AGGGAGTGGT CTTC

24

(2) INFORMATION FOR SEQ ID NO:21

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 46 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: oligonucleotide primer PD3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CGCGGATCCA ATAAGGAGGA AAAAAAATGT CACCAGATAA ACAAAT

46

(2) INFORMATION FOR SEQ ID NO:22

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: oligonucleotide primer PD4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CGCGGTACCC AGTCTCTGGA GCCGGA

26

(2) INFORMATION FOR SEQ ID NO:23

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: adapter fragment for plasmid pCJ1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

GATCTAGAAT TGTCATGTTT GACAGCTTAT CAT

33

(2) INFORMATION FOR SEQ ID NO:24

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: polylinker sequence for plasmid pCJX1-1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24

AATTCCCGGG TACCAGATCT GAGCTCACTA GTCTGCA

37

(2) INFORMATION FOR SEQ ID NO:25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 747 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: nucleic acid sequence for human GDNF

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25

TTCTCTCCCC CACCTCCCGC CTGCCCCGCGC A GGT GCC GCC GCC GGA	46
Gly Ala Ala Ala Gly	
CGG GAC TTT AAG ATG AAG TTA TGG GAT GTC GTG GCT GTC TGC	88
Arg Asp Phe Lys Met Lys Leu Trp Asp Val Val Ala Val Cys	
CTG GTG CTG CTC CAC ACC GCG TCC GCC TTC CCG CTG CCC GCC	130
Leu Val Leu Leu His Thr Ala Ser Ala Phe Pro Leu Pro Ala	
GGT AAG AGG CCT CCC GAG GCG CCC GCC GAA GAC CGC TCC CTC	172
Gly Lys Arg Pro Pro Glu Ala Pro Ala Glu Asp Arg Ser Leu	
GGC CGC CGC CGC GCG CCC TTC GCG CTG AGC AGT GAC TCA AAT	214
Gly Arg Arg Arg Ala Pro Phe Ala Leu Ser Ser Asp Ser Asn	
ATG CCA GAG GAT TAT CCT GAT CAG TTC GAT GAT GTC ATG GAT	256
Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp	
TTT ATT CAA GCC ACC ATT AAA AGA CTG AAA AGG TCA CCA GAT	298
Phe Ile Gln Ala Thr Ile Lys Arg Leu Lys Arg Ser Pro Asp	
1	
AAA CAA ATG GCA GTG CTT CCT AGA AGA GAG CGG AAT CGG CAG	340
Lys Gln Met Ala Val Leu Pro Arg Arg Glu Arg Asn Arg Gln	
5 10 15	
GCT GCA GCT GCC AAC CCA GAG AAT TCC AGA GGA AAA GGT CGG	382
Ala Ala Ala Ala Asn Pro Glu Asn Ser Arg Gly Lys Gly Arg	
20 25 30	
AGA GGC CAG AGG GGC AAA AAC CGG GGT TGT GTC TTA ACT GCA	424
Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala	
35 40 45	
ATA CAT TTA AAT GTC ACT GAC TTG GGT CTG GGC TAT GAA ACC	466
Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr	
50 55	

TCTCTCCCC CACCTCCCGC CTGCCCCGCGC A GGT GCC GCC GCC GGA

TTCCTGCTAC AGTGCAAAGA AAG 747

(C) TOPOLOGY: linear

Met Pro Glu Asp Tyr Pro Asp Gln Phe Asp Asp Val Met Asp
65 70 75

